

HISTOLOGIC CHANGES IN THE INNER EAR OF ANIMALS
EXPOSED TO X-IRRADIATION

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HISTOLOGIC CHANGES IN THE INNER EAR OF ANIMALS
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Following x-irradiation (either general or local exposure) of rabbits and guinea pigs in the region of the ear, the animals were kept under observation for some time and then killed. The x-ray doses used (total local dose: 2 x 1000 R; total general dose: 300 or 600 R) induced traumatic effects as well as pathologic changes in the middle and inner ears of these animals. The organ of Corti was the most sensitive to x-ray. Reaction to the traumatic effect could clearly be noted as labyrinthitis.

With x-irradiation of the temporal region, in addition to side effects /78* in the skin and cartilage of the pinna, there can also be changes in the middle and inner ear. These changes are little known due to the rare use of x-irradiation when there is localization of disease processes in these organs.

In order to determine the character of the morphological changes in the inner ear of animals under the influence of x-radiation in 1954-1955 we carried out experiments on rabbits and guinea pigs. Data in the literature on the effect of x-rays and radium on the ear are very scanty.

From the studies of the biological effect of ionizing radiations it is known that the most sensitive part of the cell to such radiation is the nucleus. Under the influence of irradiation there is pyknosis (condensation of chromatin) in the nucleus and karyorrhexis (disintegration of the cell nucleus), and there is vacuolization in the nucleus and protoplasm. The degree of these changes is dependent on the irradiation dose.

With respect to the differences in the effect of x-rays on different tissues, there are data on the primary resistance of the cell elements of the central nervous system and the peripheral receptors [Werner]. Nevertheless, in the experiments of I. A. Lopotko the following significant changes were discovered in the ear of white mice under the influence of the rays: hemorrhages in different parts of the ear, including hemorrhages around and within the nerve trunks supplying parts of the inner ear, detachment of the otoliths of the utricle, edema, inflammation and necrosis of the soft tissues of the labyrinth and also inflammatory exudate in the middle ear. With a dose of 12 rad, pathological changes were found both in the organ of Corti (total atrophy) and in the nerve cells of the spiral ganglion. Atrophic and degenerative changes were observed later in these same places.

*/Numbers in the margin indicate pagination of the original foreign text.

The cells of the vestibular ganglion also were subjected to degeneration two months after irradiation.

However, other authors [Thielman] did not observe inflammatory or degenerative changes in the aural labyrinth; despite such a high dose as 6-18 rad there was only capillary hyperemia and numerous hemorrhages.

With respect to the effect of radium rays, corresponding data have been published by Marx (1909), Muta (1926) and K. L. Khilov (1927). They used radium (radium bromide) in glass capillaries placed in the wall of the labyrinth. Inflammation of the middle ear, small-celled inflammatory infiltration, dilatation of the blood vessels, hemorrhages, expressed most clearly in the ductus cochlearis, and destruction of the organ of Corti were observed. According to Marx, it begins with swelling and other forms of deformation of the cells; later there is a flattening of the organ of Corti to the size of a low epithelial mound and in places to a thin strip. Defects of the nerve fibers and ganglion cells or even their complete absence also were noted.

The data in the literature, therefore, indicate that in response to the effect of radium there are degenerative-atrophic changes of the highly developed sensory epithelium and the nerve ganglion cells. With those doses which were used, the degeneration progresses without restraint but is limited to /79 the tissues directly surrounding the tube containing the radium bromide.

In Vitro Observations

Ten rabbits and ten guinea pigs were subjected to x-radiation. A dose known to be large was used to obtain the most clearly expressed changes.

Four rabbits were irradiated twice (with an interval of one day) in the region of the right ear with a dose of 1000 R (total dose of 2000 R); six rabbits were subjected to a total x-radiation of 600 R.

Five guinea pigs were subjected to local irradiation in the region of the right ear in the same dose as the rabbits; the other five guinea pigs were subjected to a total irradiation dose of 300 R.

With local exposure to x-rays (in the region of the right ear of the animal), an area 6 x 8 cm was irradiated with a skin-focus distance of 23 cm; 185 kv and 10 ma were used; a copper plate filter 0.5 mm thick was employed; the exposure required 13 minutes; the dose was 1000 R.

For the general radiation exposure the rabbits were fastened to a special stand; irradiation was in a field measuring 20 x 20 cm with a skin-focus distance of 75 cm; 180 kv and 20 ma were used; a copper plate 0.5 mm thick was employed; the exposure lasted 55.5 minutes; the dose was 600 R. In the general irradiation of the guinea pigs all the conditions were the same but the skin-focus distance was 40 cm, exposure was 17.4 minutes and the dose was 300 R.

After irradiation the animals were kept under observation for some time

and then killed.

For processing the pyramids of the temporal bones of the animals, we used post-mortem formalin fixing and biopsy fixing with a fluid containing potassium ^{di}chromate, formalin and acetic acid. The biopsy fixing was ^{done} by the method described by V. F. Undrits in a manual on the diseases of the ear, throat and nose edited by S. M. Kompaneys.

A total of 660 histologic specimens were prepared and studied. In two of the four rabbits subjected to local irradiation (region of the right ear) labyrinthitis developed on the right side: in one after three months and five days ^{and} in the second five months and four days after exposure to x-rays.

In the first rabbit the changes in the right ear amounted to atrophy of the organ of Corti, dislocation and vacuolization of its cells, accumulation of exudate in the endo- and perilymphatic cavities of the inner ear and granularity of the protoplasm of the cells of the spiral ganglion. In the second rabbit, the organ of Corti on the right (irradiated) side was destroyed; also partially destroyed were the cartilaginous formations of the vestibule and the semicircular canals; in the ductus cochlearis, utricles of the vestibule and ^{also} ~~also~~ between the walls of the bony and membranous labyrinth there was an exudate with a large quantity of cell elements; in the cavities of the middle ear there was an exudate and hemorrhages; there also was granularity of the protoplasm of the cells of the spiral ganglion (Figure 1). In the left ear of this animal there was marked atrophy of the organ of Corti (up to aplasia) and granularity of the protoplasm of the cells of the spiral ganglion.

In two other rabbits subjected to local irradiation, the histologic pictures in general were similar: in the right ear, that is, on the irradiated side, there not only was sharply manifested atrophy of the organ of Corti and dislocation and vacuolization of its remaining cells, but a thinned membrane of Corti and a deformed Reissner's membrane (locally it was absent); in the left ear the degree of expression of the changes was somewhat less. In both animals the protoplasm of the cells of the spiral ganglia (of both the right and left /80 ears) was granular; the vascular strip was thickened; in the cavities of the middle ear there was an exudate. Among the six rabbits subjected to general x-irradiation, only two of the animals developed symptoms of one-sided labyrinthitis; in one animal this happened four months after irradiation, and in the other -- after five and a half months.

Changes under general irradiation differed from the changes during local exposure to x-rays in that in the case of a general radiation trauma, labyrinthitis developed later and more slowly and its symptoms were expressed less clearly; in the right ear the histologic changes were as follows: aplasia of the organ of Corti, dislocation and vacuolization of its remaining cells, exudate in the cavities of the inner and middle ear, hemorrhages in them; granularity of the protoplasm of the cells of the spiral ganglion. In the left ear the changes were similar but there was no accumulation of exudate in the cavities of the inner ear. Since the irradiation was general, this noncorrespondence between the right and left ears must be considered random.



Figure 1. Histologic Specimen of the Ductus Cochlearis of the Right Ear of a Rabbit. Total Dose of Local Irradiation 2000 R. Labyrinthitis. Membranous Labyrinth and Organ of Corti Destroyed. In the Ductus Cochlearis There Are Hemorrhages and Exudate with a Large Number of Cell Elements. Microphotogram, Small Magnification.

In the four other rabbits the histologic changes in the ears for the most part were identical and consisted of atrophy of the organ of Corti (up to its aplasia), thinning of the membrane of Corti, granularity of the protoplasm of the cells of the spiral ganglion, a decrease of its volume, pyknosis of the nuclei, small hemorrhages under the mucosa of the tympanic cavity; in one of the rabbits there was a dislocation of the cells of the organ of Corti, deformation of Reissner's membrane and exudate in the cavities of the cochlear duct.

In guinea pigs, under both local and general irradiation, no labyrinthitis was observed. However, their total resistance to the used doses was considerably reduced: after local irradiation in two of the five animals there was a sharp loss of weight and after general exposure to x-rays three of the five guinea pigs soon died (two after nine days and one after five days).

The histologic changes in guinea pigs subjected to local irradiation were⁸¹ as follows: in the right (irradiated) ear there was aplasia of the organ of Corti, dislocation and vacuolization of its remaining cells, a noninflammatory exudate in the scala vestibuli and ductus cochlearis and also in the cavities of the middle ear, poor definition of the contours of the cells of the spiral ganglion and granularity of their protoplasm (Figure 2). In the left ear the histologic changes were the same but less clearly expressed.

The following changes were noted in the general irradiation of guinea pigs: a clearly expressed atrophy of the organ of Corti, dislocation and vacuo-



Figure 2. Histologic Specimen of the Ductus Cochlearis of the Right Ear of a Guinea Pig. Total Dose of Local Irradiation of 2000 R. Clearly Expressed Atrophy of the Organ of Corti (Aplasia); Exudate in the Ductus Cochlearis and the Scala Vestibuli. Microphotogram, Small Magnification.

lization of its cells, poor expression of the outlines of the cells of the spiral ganglion and granularity of their protoplasm, disintegration of the neuroepithelium in the region of the ampullary crest, exudate in the cavities of the middle and inner ear, and small hemorrhages in the middle ear.

Thus, both local and general exposure to large doses of x-rays caused severe atrophic and degenerative changes of the sensory formations of the inner ear, especially in the organ of Corti, in rabbits and guinea pigs. The changes were expressed more weakly on the nonirradiated side.

In some of the animals (four rabbits) there was labyrinthitis with corresponding clinical symptoms and histologic changes of the inner ear during both local and general irradiation. Due to the absence of other explicit unfavorable factors it is necessary to attribute the appearance of labyrinthitis in our experiments to the effect of x-rays, similar to the reactions of the skin and mucous membranes to irradiation.

In the literature we found no reports on cases of labyrinthitis developing in irradiated animals.

According to recent data in the literature, the cell elements of the nervous system, in contrast to the peripheral receptor formations, are the most /82 resistant to the effect of x-rays. Our experiments confirm this conclusion: whereas in the organ of Corti there were clearly expressed atrophic and degenerative changes, in the spiral ganglion these changes were expressed relatively

poorly and seemed to be more a manifestation of some basic^{protein} dysfunction. However, in the cells of the vestibular ganglion we observed no pathologic changes at all.

Our only clinical observation was for a patient with a nonkeratinizing squamous cell carcinoma of the ear (right). The patient was subjected to surgical and actinic treatment; during the period from 1948 to 1955 he received in the region of the right ear a total irradiation of 23,000 R. Hearing in the diseased ear gradually worsened and in 1955 a whisper could be heard only at distance of 0.5 m. The audiogram revealed a decrease of hearing primarily in the range of higher sounds.

In this clinical observation we can see a certain confirmation of the collected experimental data: 1) the possibility of a direct effect of x-rays on the inner ear; and 2) a predominance of the effect of x-rays on the auditory apparatus.

The results of these experiments with the irradiation of animals by x-rays make it possible for us to draw the following conclusions.

1. The x-ray doses used have a traumatic effect on the ears of these animals.
2. Pathologic changes are observed in these animals in both the inner and middle ear.
3. The organ of Corti is the most sensitive to x-rays.
4. The reaction to the traumatic effect of x-rays can attain the degree of clearly expressed labyrinthitis.

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